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**The effects of aerobic exercise on hippocampal formation volume in
schizophrenia and how to promote adherence to exercise regimens**

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vorgelegt von
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Affidavit

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Confirmation of congruency between printed and electronic version of the doctoral thesis

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List of abbreviations

ACC	Anterior cingulate cortex
AET	Aerobic endurance training
ASKU	General self-efficacy short scale
BFI-10	Big five inventory 10
BMI	Body-mass-index
BRS	Brief resilience scale
CA (1-4)	Cornu ammonis (1-4)
CI	Confidence interval
DG	Dentate gyrus
DST	Digit span test
EMI-2	Exercise motivation inventory 2
ESPRIT	Enhancing Schizophrenia Prevention and Recovery through Innovative Treatments
FDR	False discovery rate
FROGS	Functional remission of general schizophrenia scale
FSBT	Flexibility, strengthening and balance training
GAF	Global assessment of functioning scale
GPAQ	Global physical activity questionnaire
HF	Hippocampal formation
IE-4	Internal-external control belief scale
MRI	Magnetic resonance imaging
PANSS	Positive and negatives syndrome scale
PFC	Prefrontal cortex
PRISMA	Preferred reporting items for systemic reviews and meta-analyses
PROSPERO	International prospective register of systematic reviews
R1 score	Brief scale for risk-taking
RoB	Risk of bias
RoB 2	Risk-of-bias tool for randomized trials

SSA	Self-efficacy for sporting activity
VLMT	Verbal learning and memory test
WHO	World Health Organisation

List of publications

Roell, L., Fischer, T., Keeser, D., Papazov, B., Lembeck, M., Papazova, I., Greska, D., Muenz, S., Schneider-Axmann, T., Sykorova, E., Thieme, C. E., Vogel, B. O., Mohnke, S., Huppertz, C., Roeh, A., Keller-Varady, K., Malchow, B., Stoecklein, S., Ertl-Wagner, B., ... Maurus, I. (2024). Effects of aerobic exercise on hippocampal formation volume in people with schizophrenia: A systematic review and meta-analysis with original data from a randomized-controlled trial. *Psychological Medicine*, 54(15), 1–12. <https://doi.org/10.1017/S0033291724001867>

Wambsganz, A., Köpl, K., Roell, L., Fischer, T., Schwaiger, R., Hasan, A., Schmitt, A., Falkai, P., & Maurus, I. (2024). Reasons to move—A cross-sectional study to identify factors promoting regular exercise. *Frontiers in Sports and Active Living*, 6, 1515687. <https://doi.org/10.3389/fspor.2024.1515687>

Publications in revision

Köpl, K., Wambsganz, A., Röhl, L., Schwaiger, R., Fischer, T., Hasan, A., Schmitt, A., Falkai, P., & Maurus, I. (2025). *Determinants of physical activity and exercise in individuals with mental illness: Results from a large-scale online survey* [Manuscript submitted for publication]. *BMJ Open*, LMU Munich, Faculty of Psychiatry and Psychotherapy.

Your contributions to the publications

1.1 Contribution to paper I

Regarding my contribution as a shared first author, it is crucial to state that the publication essentially comprises 2 full-scale projects that were merged into one paper in order to publish in a journal with a high(er) impact factor. My project was a comprehensive meta-analysis investigating the effects of aerobic exercise interventions on hippocampal formation volumes in schizophrenia populations. Firstly, the project required formulating a research question and objectives using the PICO framework (P: Schizophrenia, I: Aerobic exercise, C: e.g. table football, O: Hippocampal formation volume) as well deciding upon in- and exclusion criteria including but not limited to study design, populations, interventions and outcomes. The next step involved study pre-registration with PROSPERO in order to guarantee transparency, which included the following aspects: background & rationale, research question(s), in- and exclusion criteria, search strategies, data extraction, quality assessment as well as a plan for statistical analysis. Subsequently, a comprehensive literature search was conducted using the following databases: Cochrane, PubMed, Web of Science, ISRCTN and Embase in search of published, unpublished and grey literature. Screening and selection were carried out by Lukas Röhl and myself, so as to minimize bias and resolve discrepancies through consensus. Next, data extraction comprised sample sizes, means, standard deviations, risk of bias was assessed using Cochrane's "risk-of-bias tool for randomized trials" (RoB 2) and statistical analysis was performed using "Comprehensive Meta-Analysis Software" (V4). Moreover, statistical analysis entailed sensitivity analysis, assessment of heterogeneity (Cochran's Q , Higgins I^2), publication bias (funnel plot, Egger's regression coefficient, Begg and Mazumdar's rank correlation value) and in case of publication bias violation a Duval and Tweedie trim-and-fill analysis. PRISMA guidelines were adhered to when reporting and interpreting results (flow diagrams, forest and funnel plots).

As previously mentioned, the meta-analysis was then merged with Lukas Röhl's project concerning the effects of aerobic exercise interventions on hippocampal subfields as opposed to the hippocampal formation as a whole (meta-analysis). Subsequently, I proceeded to revise the entire manuscript grammatically and linguistically, while also checking for sound and coherent theory, methodology and discussion in both parts.

1.2 Contribution to paper II

Prior to reviewing and editing the manuscript, I examined and adjusted crucial aspects of the questionnaire that was used to collect essential data subsequently used in the study's analysis. Thereby ensuring that said collected data was sound, reliable and valid. Steps included ensuring that objectives were clear, that valid and/or reliable questions and response items were chosen, and that these were clear in their intention and free of bias to the best of their abilities. Subsequently, I proceeded to revise the manuscript grammatically and linguistically while also checking for sound and coherent theory, methodology and discussion.

2. Introduction summary

2.1 Schizophrenia and why we require exercise regimens as add-on interventions

Schizophrenia frequently manifests as a chronic and disabling psychiatric disorder in late adolescence or early adulthood and entails a wide variety of both positive and negative symptoms (James et al., 2018). Positive symptoms refer to an excess and/or a disturbance of normal functioning (e.g. hallucinations, delusions, disorganized thinking and/or motor behavior), whereas negative symptoms can be categorized into two key factors, namely “diminished expression” (e.g. blunted affect, alogia) and “avolition/apathy” (e.g. avolition, asociality, anhedonia) as well as secondary negative symptoms such as depression, medical comorbidities, antipsychotic-related sedation, substance misuse, environmental deprivation and stigma, to name several (Correll & Schooler, 2020).

On the one hand, available antipsychotics offer viable and often efficient means of treating positive symptoms (Nielsen et al., 2015). On the other hand, negative symptoms and cognitive deficits often persist due to limited treatment options despite increased understanding of the etiology, epidemiology, biology, and psychopharmacology of schizophrenia (Carbon & Correll, 2014). This is particularly tragic due to the often-chronic nature of schizophrenia and the fact that negative symptoms disproportionately contribute to impaired social and occupational functioning, thereby preventing meaningful and sustainable recovery on a functional and community level (Fusar-Poli et al., 2015). Meta-analytic evidence shows that only one out of seven patients with schizophrenia meets criteria for recovery and shows significant improvements in social and clinical outcomes over a time-period of at least 2 years (Jääskeläinen et al., 2012). Managing negative symptoms in a clinical setting includes minimizing medication side-effects that may aggravate negative symptoms, adjusting or switching medication (e.g. cariprazine as a dopamine D₃/D₂ receptor partial agonist and serotonin 5-HT_{1A} partial agonist), treating

comorbid medical/psychiatric conditions, seeing a psychologist for psychosocial interventions, as well as encouraging self-care, environmental stimulation and social interactions (Correl & Schooler, 2020). However, the effectiveness of said interventions in negative symptom reduction remains limited as well as predominately bound to the clinical setting, which emphasizes the lack of or rather the necessity of postulating and investigating novel treatments for negative symptom reduction outside of hospital and in the long run (Vita & Barlati, 2018).

One such treatment or intervention that has attracted attention and shown promising results in the past years is exercise regimens. Meta-analyses have concluded that exercise is effective in alleviating and/or optimizing the following symptoms/domains in people with schizophrenia: negative symptoms, cognitive and global functioning, as well as quality of life (Dauwan et al., 2016). Moreover, exercise is crucial in improving overall health and well-being including but not limited to weight, blood pressure, cholesterol, and so forth. This is of essence in schizophrenia, as those suffering have higher morbidity and mortality rates compared to the general population due to higher rates of cardiovascular disease, metabolic syndrome and diabetes (Vancampfort et al., 2015). Patients with schizophrenia often exhibit an array of unhealthy habits; they are more likely to smoke, exercise less and adhere to unhealthy diets when compared to the general population (Sagud et al., 2018). So much so that the World Health Organisation (WHO) recommends interventions for those suffering from severe mental illness and at risk for cardiovascular events in its guideline “Management of Physical Health Conditions in Adults with Severe Mental Disorders” (World Health Organization, 2018). Overall, it is important to state that physical exercise is crucial in maintaining physical health and well-being in the general population as well as specifically in those suffering from mental disorders, and even more so in individuals with schizophrenia due to unhealthy habits associated with the disease itself but also the side-effects of anti-psychotic medication. So, what is the current state

of research on exercise interventions in schizophrenia and what are the hypothesized underlying neurobiological mechanisms of action/change?

2.2 Current state of research and the underlying neurobiological mechanisms of action

Generally speaking, it has been hypothesized that exercise increases neuroplasticity at morphological and functional levels by means of modifying the expression of neurotrophic factors and neurotransmitters in the brain (Maurus et al., 2021). More specifically, a review conducted by Maurus et al. (2019) summarizes the many structural, cellular and molecular mechanisms possibly associated with the effects of aerobic exercise interventions in schizophrenia, as shown in animal models but also in humans, including but not limited to: an increase in hippocampal formation and gray matter volume, improved white matter connectivity, adaptations and enhancements in epigenetics and neurogenesis, increased cerebral blood flow/angiogenesis, elevated levels of growth factors and neurotransmitters including serotonin, noradrenaline, dopamine and glutamate, normalization of the HPA-axis, oligodendrocyte differentiation as well as reduced inflammation. Said postulated mechanisms and/or affected brain regions are also those often impaired in schizophrenia, as studies have shown that compared to healthy controls individuals with schizophrenia have smaller hippocampal formation, gray and white matter volumes especially in the bilateral insula, anterior cingulate cortex (ACC), thalamus, medial prefrontal cortex (PFC) and amygdala (Maurus et al., 2022). Said brain regions are associated with cognitive deficits in general and specifically with emotional regulation, motivation, arousal, attention, learning and memory (Guessoum et al., 2020).

The hippocampus and/or the hippocampal formation and its subfields have been of particular interest as deterioration in this region has been associated with several psychiatric/neuro-

logical disorders, as stated above, while also being of particular importance to declarative learning, memory formation, verbal short- and long-term memory, processing speed, pattern separation, spatial processing and increased severity of positive and negative symptoms (Ho et al., 2017 & Nakahara et al., 2018). Moreover, aerobic exercise has been shown to be associated with retention of or even an increase in hippocampal formation volume, which in turn correlates with improved cognition, e.g. short-term memory, working memory and overall functioning (Falkai et al., 2021).

However, evidence as well as study designs regarding exercise intervention protocols and their effects on hippocampal formation volumes remain largely heterogeneous and somewhat inconclusive. In a groundbreaking study, Pajonk et al. (2010) were the first to report an increase in hippocampal volume in individuals with schizophrenia as well as healthy controls following exercise interventions. Khonsari et al. (2022) and Woodward et al. (2018), for example, were able to replicate said findings, whereas others, such as Malchow (2016) or Scheewe et al. (2013) reported null results regarding the effects of exercise on hippocampal volumes in patients with schizophrenia. Moreover, in their meta-analysis, Firth et al. (2018) showed no effect on total hippocampal formation volume but an increase in the left hippocampus only following aerobic exercise interventions in individuals with mental illness and healthy controls.

2.3 Rationale for a meta-analytic perspective

Considering the often-chronic nature of schizophrenia and the devastating effects of negative symptoms on cognition and the physical health of those affected, it is crucial to investigate and evaluate the body of literature covering (exercise) interventions aimed at improving global functioning and cognition. As previously stated, it has been hypothesized and several studies have shown that the beneficial effects of aerobic exercise on cognition in schizophrenia may be mediated by neuroplasticity and/or increases in hippocampal formation volume. However,

due to the heterogeneous intervention designs, methodology, findings and the lack of systematic reviews, it was crucial to synthesize and thoroughly summarize the current state of literature. Thereby better understanding if the effect of exercise on global hippocampal formation is indeed significant or if future research needs to dive deeper, for example, by taking a closer look at hippocampal subfields or specific subpopulations amongst those with schizophrenia.

2.4 How to promote adherence to exercise regimens

Engaging in physical activity on a regular basis has a wide array of benefits including but not limited to reducing the risk for cardiovascular disease, diabetes and colorectal cancer, while also reducing the risk for and occurrence of psychiatric conditions such as depression and/or anxiety (Schuch & Vancampfort, 2021; Warburton & Bredin, 2019). The World Health Organization not only recommends exercise regimens for those suffering from severe mental illness and at risk for cardiovascular events, but also at least 150 minutes of moderate physical activity or 75 minutes of vigorous physical activity for the general population (World Health Organization, 2020). Still, only roughly 30% of adults in the European Union are able to meet these goals on a regular basis (Eurostat, 2022).

When considering how important physical activity is to the general population and specifically to those with psychiatric conditions, the need to investigate factors promoting adherence to regular exercise becomes more than evident. Numerous factors, such as personality traits (e.g. extraversion), locus of control (intrinsic vs. extrinsic), childhood sport history, self-efficacy, and others have been proposed in recent literature and were thoroughly examined throughout this thesis (Elbe, 2021; Müller, 2023).

3. Abstract (German):

Hintergrund: Beeinträchtigung der Hippocampusformation sind ein Kernmerkmal der Schizophrenie und gehen häufig mit eingeschränkter Kognition sowie einer schlechten klinischen Prognose einher. Aerobe Sportinterventionen stellen seit mehr als einem Jahrzehnt eine vielversprechende Intervention zur Besserung der kognitiven Fähigkeiten und des klinischen Outcomes dar. Jedoch zeigen Interventionsprotokolle sowie Studienergebnisse weiterhin eine erhebliche Heterogenität auf. Deshalb erstellten wir eine Meta-Analyse, die die bestehende Literatur zu den Effekten von aeroben Sportinterventionen auf die Volumina der Hippocampusformationen zusammenfasst. Darüber hinaus wurde analysiert, ob eine solche Volumenzunahme mit einer Verbesserung von kognitiven und/oder klinischen Ergebnissen einhergeht und welche Faktoren körperliche Aktivität positiv beeinflussen.

Methodik: Die Meta-Analyse umfasste sechs Studien und verglich den Effekt von aeroben Sportinterventionen auf das Volumen der Hippocampusformation in 186 Individuen mit Schizophrenie vs. Kontrollprobanden (100 männlich, 86 weiblich). Des Weiteren analysierten wir Daten aus der ESPRIT-Studie mit 29 Teilnehmern mit Schizophrenie (20 männlich, 9 weiblich), die jeweils ein sechs-monatiges aerobes Sportprogramm absolvierten. Außerdem wurden anhand von 1119 gesunden Teilnehmern Faktoren, die die körperliche Aktivität fördern, untersucht.

Ergebnisse: Weder die ursprüngliche noch die explorative Meta-Analyse ergaben signifikante Unterschiede bezüglich der Effekte von aeroben Sportinterventionen auf die Volumina der Hippocampusformation. Im Gegensatz dazu zeigten die ESPRIT-Daten eine Zunahme der Volumina in bestimmten Subfeldern der Hippocampusformation nach Sportinterventionen, darunter das Ammonshorn und der Gyrus Dentatus. Ob Menschen regelmäßig Sport treiben, hängt von ihrem sozioökonomischen Hintergrund, dem sportlichen Verhalten ihrer Familie sowie der Verfügbarkeit von Sporteinrichtungen in ihrer Umgebung ab.

Fazit: Obwohl die Meta-Analysen keinen signifikanten Effekt von aeroben Sportinterventionen auf die Volumina der Hippocampusformation zeigten, deuten Ergebnisse aus der ESPRIT-Studie darauf hin, dass neuroplastische Prozesse in einzelnen Subfeldern gefördert werden können. Dies unterstreicht die Wichtigkeit, Patientenuntergruppen zu identifizieren, die von maßgeschneiderten Interventionen profitieren könnten sowie niedrigschwellige und kostengünstige Sportangebote, die sozial benachteiligte Gruppe einbeziehen, anzubieten.

4. Abstract (English):

Background: Deteriorations in the hippocampal formation are a hallmark of schizophrenia and associated with impaired cognition as well as poor clinical outcomes. In the past decade, aerobic exercise interventions have gained interest as a promising therapeutic intervention aimed at increasing global hippocampal volume and improving clinical, cognitive and global functioning outcomes. However, intervention protocols and findings remain heterogeneous and inconsistent. Therefore, a systemic review and meta-analysis was performed assessing whether aerobic exercise leads to increases in global hippocampal volume. Moreover, the thesis covered whether such increases are also associated with improved cognitive and/or clinical outcomes as well as factors promoting and improving adherence to exercise regimens.

Methods: The meta-analysis comprised six studies and compared aerobic exercise on total hippocampal formation volume to control conditions in a total of 186 individuals with schizophrenia (100 males, 86 females). Moreover, an additional exploratory analysis including nine studies was performed. In addition, we analysed original data from a multicenter randomized controlled trial (ESPRIT), which included 29 participants with schizophrenia (20 males, 9 females) who each completed a six-month aerobic exercise program. Moreover, assessing factors promoting physical activity comprised a total of 1119 mentally healthy individuals.

Results: Neither the original meta-analysis nor the exploratory analysis revealed significant effects of aerobic exercise interventions on global hippocampal formation volume. In contrast, the original trial data demonstrated significant increases in volume in select hippocampal subfields, most prominently within the cornu ammonis and dentate gyrus. Adhering to physical activity was associated with socioeconomic status, whether one's family exercises and the availability of facilities in one's vicinity.

Conclusions: Although meta-analytic findings did not demonstrate significant effects of aerobic exercise on global hippocampal formation volumes, our findings suggest that neuroplasticity may be promoted within specific hippocampal subfields. Thereby, emphasizing the importance of identifying patient subgroups that may benefit from targeted interventions as well as promoting low-threshold and low-cost opportunities focused on disadvantaged social groups for engaging in physical activity.

Paper I

Psychological Medicine

cambridge.org/psm

Review Article

*These authors contributed equally.

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Effects of aerobic exercise on hippocampal formation volume in people with schizophrenia – a systematic review and meta-analysis with original data from a randomized-controlled trial

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Abstract

Background. The hippocampal formation represents a key region in the pathophysiology of schizophrenia. Aerobic exercise poses a promising add-on treatment to potentially counteract structural impairments of the hippocampal formation and associated symptomatic burden. However, current evidence regarding exercise effects on the hippocampal formation in schizophrenia is largely heterogeneous. Therefore, we conducted a systematic review and meta-analysis to assess the impact of aerobic exercise on total hippocampal formation volume. Additionally, we used data from a recent multicenter randomized-controlled trial to examine the effects of aerobic exercise on hippocampal formation subfield volumes and their respective clinical implications.

Methods. The meta-analysis comprised six studies that investigated the influence of aerobic exercise on total hippocampal formation volume compared to a control condition with a total of 186 people with schizophrenia (100 male, 86 female), while original data from 29 patients (20 male, 9 female) was considered to explore effects of six months of aerobic exercise on hippocampal formation subfield volumes.

Results. Our meta-analysis did not demonstrate a significant effect of aerobic exercise on total hippocampal formation volume in people with schizophrenia ($g = 0.33$ [-0.12 to 0.77], $p = 0.15$), but our original data suggested significant volume increases in certain hippocampal subfields, namely the cornu ammonis and dentate gyrus.

Conclusions. Driven by the necessity of better understanding the pathophysiology of schizophrenia, the present work underlines the importance to focus on hippocampal formation subfields and to characterize subgroups of patients that show neuroplastic responses to aerobic exercise accompanied by corresponding clinical improvements.

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segmentation. Moreover, it was required that studies were published in English language and included an adult participant sample 18+ years of age.

Risk of bias and quality assessment

The most recent edition of the Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess risk of bias (Sterne et al., 2019). The tool encompasses five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Based on answers to signaling questions, an algorithm determined the extent of bias relevant to a particular domain as well as an overall bias score ranging from 'low risk of bias' to 'some concerns' and 'high risk of bias' (online Supplementary Figs S1 and S2). Both TF and LR completed the risk of bias assessment using the RoB 2.0 excel template. Inconsistencies were resolved by means of discussion.

Data extraction

Our primary outcome was the change in total hippocampal formation volume from pre- to post-intervention. The following data were extracted independently from included reports by TF and LR: sample sizes, means and standard deviations of primary outcome data prior to and post aerobic exercise interventions for the experimental and control groups. If said data were not made available in the initial report, authors were contacted by either TF or LR.

Statistical analysis

Comprehensive meta-analysis software (V4) was used to conduct random-effects meta-analyses (Borenstein, 2022) based on all trials with control condition comparing the effects on hippocampal formation volume in an aerobic exercise intervention to a study-specific control group. Hedges' g statistic was computed using intervention effect sizes (differences between intervention and control groups) for the primary outcome measurement, as were 95% confidence intervals (CIs). Effect sizes expressed as Hedges' g were classified as small ($0.2 \leq g < 0.5$), medium ($0.5 \leq g < 0.8$), or large ($g \geq 0.8$). A sensitivity analysis was conducted by means of removing one study at a time in order to assess robustness of observed effects. Heterogeneity was assessed using Cochran's Q and Higgins' I^2 , which can be divided into considerable (>75%), substantial (50–75%), moderate (30–50%), and low (< 30%). Publication bias was addressed via producing a funnel plot and assessing asymmetry using Egger's regression coefficient as well as determining Begg and Mazumdar's rank correlation value with $p < 0.05$ indicative of bias (Begg & Mazumdar, 1994; Egger, Davey Smith, Schneider, & Minder, 1997). In case of significant publication bias, a Duval and Tweedie trim-and-fill analysis was utilized (Duval & Tweedie, 2000). Moreover, in exploratory intention, we conducted a second meta-analysis which included studies without control conditions (Rosenbaum et al., 2015; Woodward et al., 2018) and underaged participants (Dean et al., 2017). This analysis was based on all available studies comparing the HF volume prior to the aerobic exercise intervention with the volume after the aerobic exercise intervention. The rationale behind the exploratory analysis was the limited number of studies surrounding the effect of aerobic exercise compared to a control condition on HF volume in schizophrenia and the low risk of placebo effects when investigating HF volume as a standalone outcome.

Randomized-controlled trial

Study design and sample

The data presented here originate from the Enhancing Schizophrenia Prevention and Recovery through Innovative Treatments (ESPRIT) C3 study (NCT03466112, <https://clinicaltrials.gov/ct2/show/NCT03466112?term=NCT03466112&draw=2&rank=1>). The ESPRIT C3 study is a multicenter randomized-controlled trial that investigates the effects of aerobic exercise on multiple health outcomes in people with schizophrenia. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the ethics committee of the medical faculty of the Ludwig-Maximilians-University Munich (approval number: 706-15).

In total 180 participants gave written informed consent and were randomly assigned to either an aerobic endurance training (AET) or to a flexibility, strengthening and balance training (FSBT). Supervised by a sport scientist, both groups exercised up to three times per week, for approximately 40–50 min per session, for a total duration of six months. Patients in the AET group cycled on a stationary bicycle ergometer at a moderate exercise intensity which was determined by a lactate threshold test prior to the onset of the intervention. In the FSBT group, patients performed exercises covering stretching, mobility, stability, balance, and relaxation (Liu-Ambrose et al., 2010). Ninety nine subjects initially agreed to undergo MRI sessions, but evaluable structural T1-weighted MR images from which HF subfield volumes could be computed at baseline and post-intervention were available for only 29 participants (9 in the AET group, 20 in the FSBT group). Table 1 depicts the sample characteristics. Details of the ESPRIT C3 study are described in the supplemental information and in the corresponding study design publication (Maurus et al., 2020).

Structural MRI data and clinical variables

The hippocampal module of FreeSurfer v7.2 (Iglesias et al., 2015) was used to compute the volumes of HF subfields at a spatial isotropic resolution of 0.8 mm^3 at study site Munich and 1 mm^3 at study sites Mannheim and Berlin. Based on the proportion method (O'Brien et al., 2011), HF volumes were corrected via intracranial volume across all subjects and sessions and volumes of bodies and heads were summed up for each subfield. Because the FreeSurfer segmentation of all HF subfields based on MRI scans at a spatial isotropic resolution of 1 mm^3 has been criticized due to issues regarding the detection of the boundaries between subfields (Wisse et al., 2021), we conducted an additional analysis segmenting the HF only into head, body, and tail.

The Positive and Negative Syndrome Scale (PANSS) was administered to assess positive and negative symptoms, and total symptom severity (Kay, Fiszbein, & Opler, 1987). Verbal semantic long-term memory comprised a composite score of the sixth and seventh run of the Verbal Learning and Memory Test (VLMT), whereas the average of the first and interference run was utilized to cover verbal semantic short-term memory (Helmstaedter & Durwen, 1990). The backward version of the Digit Span Test (DST) was employed to target verbal working memory (Tewes, 1994). The Global Assessment of Functioning scale (GAF) and the Functional Remission of General Schizophrenia scale (FROGS) were applied to assess general functioning (Endicott,

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Table 1. Sample characteristics

	AET <i>n</i> = 9 (31.0%) (<i>n</i> / mean ± s.d.)	FSBT <i>n</i> = 20 (51.6%) (<i>n</i> / mean ± s.d.)	
Study site			$p_{\text{fisher}} = 0.161$
Munich	6 (66.7%)	17 (85.0%)	
Mannheim	3 (33.3%)	1 (5.0%)	
Berlin	0 (0.0%)	2 (10.0%)	
Sex			$p_{\text{fisher}} = 1.000$
Female	3 (33.3%)	6 (30.0%)	
Male	6 (66.7%)	14 (70.0%)	
Age (years)	34.67 ± 12.29	39.40 ± 11.25	$p_{\text{wilcox}} = 0.299$
PANSS at baseline (t0)			
Positive	10.22 ± 3.03	10.65 ± 3.70	$p_{\text{wilcox}} = 1.000$
Negative	11.56 ± 4.95	12.10 ± 3.60	$p_{\text{wilcox}} = 0.477$
Total	45.44 ± 12.93	46.45 ± 9.42	$p_{\text{wilcox}} = 0.539$
Chlorpromazine equivalents	291.96 ± 151.00	438.23 ± 246.76	$p_{\text{wilcox}} = 0.150$
Education (years)	12.33 ± 3.35	16.25 ± 4.84	$p_{\text{wilcox}} = 0.064$
Total number of trainings	41.11 ± 16.34	35.70 ± 18.25	$p_{\text{wilcox}} = 0.396$

AET, aerobic endurance training; FSBT, flexibility, strengthening and balance training; PANSS, Positive and Negative Syndrome Scale; p_{fisher} , p value of Fisher's exact test for categorical data; p_{wilcox} , p value of Wilcoxon signed-rank test for numeric data; s.d., standard deviation. The sample sizes per group refer to the number of participants that were considered for the statistical data analysis.

Spitzer, Fleiss, & Cohen, 1976; Llorca et al., 2009). Further details on MRI data acquisition (online Supplementary Table S2), processing, and quality control procedures, as well as on the cognitive test batteries are provided in the supplemental information.

Statistical analysis

Statistical analysis was performed with Rstudio v1.4.1717 based on R v4.2.2 (R Core Team, 2021; RStudio Team, 2020) and visualizations were created with *ggplot2* (Wickham, 2016).

To investigate the effect of AET on HF subfield volumes in comparison to FSBT (2nd research question), linear mixed effect models for repeated measures were calculated. Group (AET, FSBT), time (t0: baseline, t6: six months), the group × time interaction, age, sex, chlorpromazine equivalents, number of trainings, volume at baseline, study site (Munich, Mannheim, Berlin), and hemisphere (left, right) were included as predictors, while the corresponding five subfield volumes served as dependent variables. p values of the factor time and the group × time interaction were adjusted separately across the five linear mixed models using the false discovery rate (FDR) method (Benjamini & Hochberg, 1995). In case of a significant group × time interaction ($p_{\text{fdr}} < 0.05$) Tukey post-hoc tests within groups and between sessions were conducted.

Regarding the potential effects of individual changes in HF subfield volumes on clinical outcomes (3rd research question), we computed multiple linear regression models to examine the general associations between changes in HF subfield volume and changes in psychiatric symptoms, cognition, and functioning. Respective corresponding subfield volume differences between t0 and t6, group, age, sex, chlorpromazine equivalents, training number, study site, and years of education served as predictors. The difference in the corresponding behavioral scores between t0 and t6 was utilized as the dependent variable. p values of the volume differences were FDR-corrected.

Results

Search results, included studies and participant details

As shown in Fig. 1, a total of 532 records were identified across five platforms. After removal of 400 duplicates, TF and LR screened 132 titles and abstracts, based on which an additional 120 studies were excluded. Of the remaining 12 records, 2 were not retrievable, 2 control conditions collapsed during primary analysis due to small sample sizes, 1 report included patients under the age of 18, and another only reported particular HF subfields. Thus, a total of six records were included in the primary analysis. The overall sample comprised 186 patients, 92 of which were assigned to aerobic exercise and 94 to control conditions. In total, 46% identified as female ($n = 86$) and 54% as male ($n = 100$), patients' mean age ranged from 24.6 to 39.3, and attrition rates from 0% to 79%. Studies were conducted in Germany (3x), Hong Kong, Iran, and the Netherlands (Khonsari et al., 2022; Lin et al., 2015; Malchow et al., 2016; Pajonk et al., 2010; Scheewe et al., 2013). Detailed patient and intervention study characteristics included in the meta-analyses can be found in online Supplementary Table S1. Risk of bias assessment suggested high concerns for three reports including our original data due to high attrition rates (Lin et al., 2015; Scheewe et al., 2013). Detailed results of the RoB analysis can be found in online Supplementary Figs S1 and S2.

Effect of aerobic exercise on global hippocampal formation volume assessed in meta-analysis

As shown in Fig. 2a, the between-groups random-effects meta-analysis ($k = 6$) revealed a small to medium but non-significant effect of exercise interventions on global hippocampal formation volume (Hedges' $g = 0.33$, 95% CI -0.12 to 0.77 , $p = 0.15$). Heterogeneity was substantial ($Q = 11.52$, $df = 5$, $p = 0.04$, $I^2 = 56.58$), whereas publication bias was non-significant (Kendall's $\tau = 0.27$, $p = 0.45$). A funnel plot (online Supplementary Fig. S3), explored for asymmetry by means of Egger's Test, confirmed a lack of publication bias (Egger's intercept = 3.31, s.e. = 4.72, $p = 0.52$). Via removing one study at a time, the effect size of aerobic exercise on hippocampal volume ranged from 0.10 to 0.43.

As illustrated in Fig. 2b, the within-group random-effects meta-analysis ($k = 9$) revealed a small but non-significant effect of exercise interventions on global hippocampal formation volume in schizophrenia and related disorders (Hedges' $g = 0.19$, 95% CI -0.05 to 0.42 , $p = 0.11$). Heterogeneity was substantial ($Q = 23.08$, $df = 8$, $p < 0.003$, $I^2 = 65.34$), whereas publication bias was non-significant (Kendall's $\tau = 0.42$, $p = 0.12$). A funnel plot (online Supplementary Fig. S4), explored for asymmetry by means of Egger's Test, confirmed a lack of publication bias

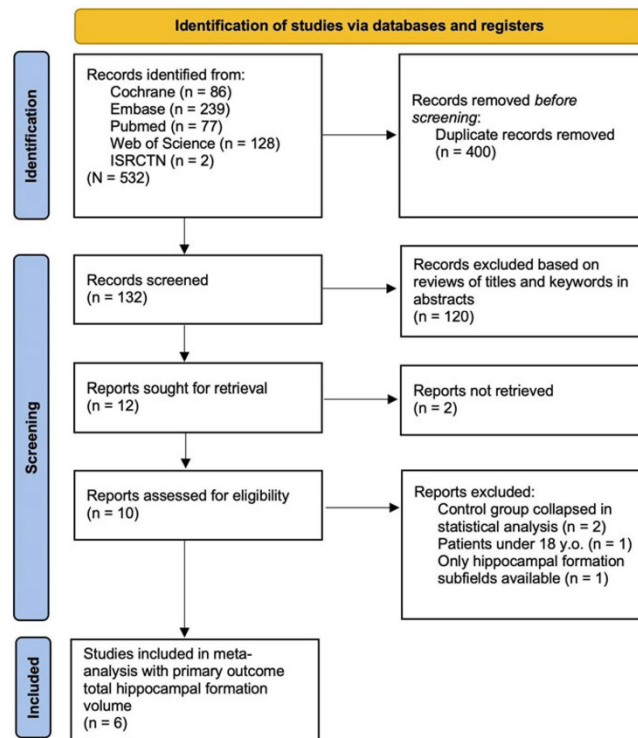


Figure 1. PRISMA flow diagram showcasing the process of identifying literature with total hippocampal formation volume as the primary outcome. A total of 6 studies were included in the meta-analysis.

(Egger's intercept = 2.98, s.e. = 3.22, $p = 0.39$). Via removing one study at a time, the effect size of aerobic exercise on hippocampal volume ranged from 0.06 to 0.23. All test statistics are available in online Supplementary Table S3.

Effect of aerobic exercise on hippocampal formation subfield volumes assessed in RCT

After FDR correction, we observed significant effects for the factor time and group \times time interaction for the following subfields: CA1 ($F = 5.11$, $p_{FDR} = 0.033$), CA2/3 ($F = 7.62$, $p_{FDR} = 0.033$), CA4 ($F = 5.29$, $p_{FDR} = 0.033$), and DG ($F = 5.67$, $p_{FDR} = 0.033$). Thus, indicating significant differences in volume changes between AET and FSBT groups over time regarding all subfields except for the subiculum. Tukey post-hoc tests revealed significant volume increases between timepoints t_0 and t_6 for CA1 ($d = 0.89$, CI [0.22–1.55], $p_{Tukey} = 0.009$), CA2/3 ($d = 1.27$, CI [0.61–1.93], $p_{Tukey} < 0.001$), CA4 ($d = 1.06$, CI [0.40–1.73], $p_{Tukey} = 0.002$), and DG ($d = 1.04$, CI [0.38–1.70], $p_{Tukey} = 0.002$) in the AET, but not in the FSBT group. Figure 3 illustrates the effects on HF volumes in both exercise groups and Fig. 4 visualizes the subfields CA1–4 and the DG.

We did not observe any significant effects for the factor hemisphere (CA1: $p = 0.864$, CA2/3: $p = 0.658$, CA4: $p = 0.335$, DG: $p = 0.392$), suggesting that volume changes occur bilaterally to the same extent.

As part of our additional analysis, Tukey post-hoc tests indicated significant volume increases in the aerobic exercise group between timepoint t_0 and t_6 for the hippocampal head ($d = 0.86$, CI [0.20–1.53], $p_{Tukey} = 0.010$) and body ($d = 1.16$, CI [0.50–1.82], $p_{Tukey} = 0.001$), but not for the tail ($d = 0.50$, CI [−0.16 to 1.16], $p_{Tukey} = 0.137$).

Clinical relevance of changes in HF volumes online Supplementary Table S4 and Figs S7, S8 and S9 summarize the full test statistics of the multiple linear regressions and the associations between changes in HF subfield volumes and changes in symptoms, cognition, and functioning, respectively. No stable correlations between longitudinal volumetric and psychopathological or cognitive changes were observed.

Discussion

Our meta-analysis reveals that there was no significant effect of aerobic exercise on total HF volume. Rather, preliminary data from our randomized-controlled trial suggested that aerobic exercise may lead to significant volume increases in certain HF subfields, namely CA1, CA2/3, CA4, and DG. However, the clinical impact of said volume changes remains subject to further investigation.

Structural deteriorations within the HF play a key role in the pathophysiology of schizophrenia and contribute to cognitive

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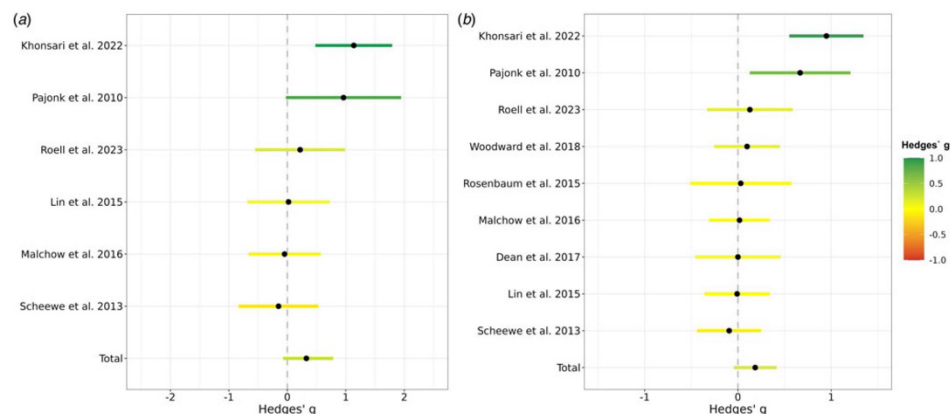
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Figure 2. Effects of aerobic exercise on total hippocampal formation volume in people with schizophrenia. (a) Meta-analysis based on all trials with control condition comparing the effects on hippocampal formation volume in an aerobic exercise intervention to a study-specific control group. A positive Hedges' g indicates that the volume increase in the aerobic exercise group was higher than in the control group. The 95% confidence intervals are represented by the colored lines. The pooled effect across all available studies is shown at the bottom and is labeled with 'Total'. Roell et al. (2024) refers to the original data presented here. (b) Meta-analysis based on all available studies comparing the hippocampal formation volume prior to the aerobic exercise intervention with the volume after the aerobic exercise intervention. A positive Hedges' g indicates that there was a volume increase from baseline to the end of the intervention within the aerobic exercise group. The lines reflect the 95% confidence intervals. The pooled effect across all available studies is shown at the bottom and is labeled with 'Total'. Roell et al. (2024) refers to the original data presented here.

deficits as well as positive and negative symptom severity (Adriano et al., 2012; Antoniadis et al., 2018; Brosch et al., 2022; Brugger & Howes, 2017; Haukvik et al., 2018; Ho et al., 2017; Honea et al., 2005; Khalil et al., 2022; Nakahara et al., 2018, 2020; Opel et al., 2020; Pijnenborg et al., 2020; van Erp et al., 2016). Therefore, the implementation of interventions that promote hippocampal health constitute an essential approach towards improving treatment outcomes in schizophrenia. Although our meta-analysis did not demonstrate a significant effect of aerobic exercise on HF volume in people with schizophrenia, a noticeable trend in favor of aerobic exercise *v.* control conditions was observable. This is in line with previous meta-analyses conducted among various populations suggesting trends towards aerobic exercise-induced volume increases of the total HF (Firth et al., 2018; Li et al., 2017), but heterogeneity between studies is high. For instance, the included trials differ in several important properties such as the duration and the exact type of the utilized aerobic exercise programs, the kind of control group or the clinical status of the underlying study population. We systematically reviewed these properties, aiming at identifying a pattern that may explain why certain trials observe HF volume increases and others do not, but based on the available information no stable and systematic pattern was detectable. Hence, so far, we can only conclude that aerobic exercise interventions in people with schizophrenia may not consistently lead to HF volume increases on a group level, but rather affect HF volumes only under certain conditions:

Firstly, temporally restricted aerobic exercise interventions in the context of scientific studies may not be sufficient to observe stable HF volume increases. Instead, large-scale evidence demonstrates that an increased HF volume in healthy subjects is associated with a higher aerobic fitness level which in turn depends on the individual's longitudinal engagement in aerobic exercise (Wittfeld et al., 2020). Our previous cross-sectional findings in people with

schizophrenia support this notion (Maurus et al., 2022a, 2022b), insofar as improvements of aerobic fitness during temporarily restricted aerobic exercise interventions have been linked to more pronounced increases of HF volume (Pajonk et al., 2010). Correspondingly, a recent meta-analysis comprising studies of various populations suggested that aerobic exercise interventions with a minimum duration of at least six months lead to more consistent increases in HF volume (Wilckens et al., 2021). Hence, we conclude that stable increases in HF volume as elicited by aerobic exercise are subject to long-term processes not always observable across the whole study population in the context of time-restricted intervention studies. Therefore, future cohort studies examining the long-term disease course of schizophrenia should collect measures of physical activity and fitness to better understand how frequently and over what period of time aerobic exercise should be performed to observe stable restorative effects on the HF volume across the whole study sample.

Second, however, aerobic exercise-induced HF volume increases can still be achieved within a shorter period of time (Khonsari et al., 2022; Pajonk et al., 2010), which may be attributable to the respective sample characteristics. Accordingly, previous evidence indicates that both a higher general polygenic risk for schizophrenia and a higher genetic burden associated with oligodendrocyte precursor cells and radial glia inhibit neuroplasticity within the HF during aerobic exercise (Papiol et al., 2017, 2019). These findings emphasize that certain genetic subgroups of patients are less likely to benefit from aerobic exercise interventions, which may in turn partially explain a lack of significance in observed effects on the group level. Hence, future research should identify multimodal factors that explain why certain patients with schizophrenia reveal increases in HF volume and others do not in order to enable individualized aerobic exercise treatments in future health care.

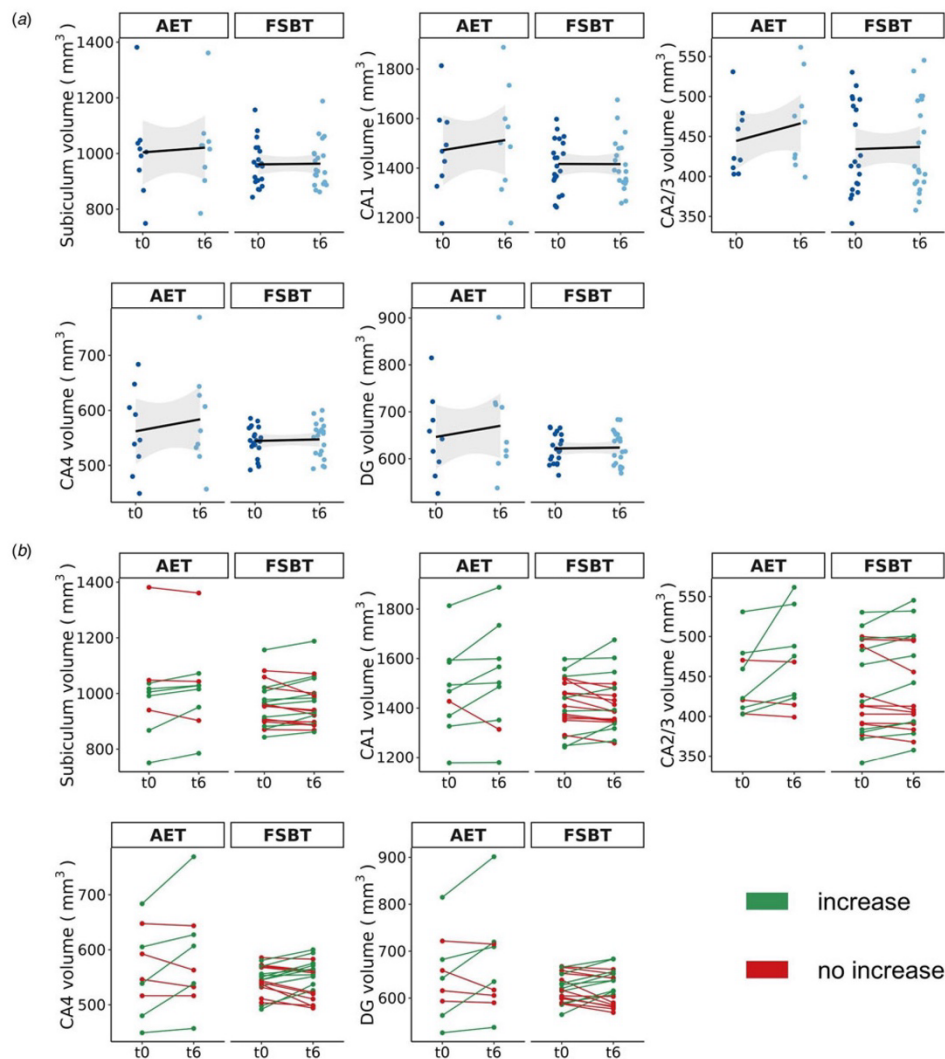


Figure 3. Exercise-induced volume changes of the HF subfields. AET, aerobic endurance training; FSBT, flexibility, strengthening and balance training; CA, cornu ammonis; DG, dentate gyrus; t0, baseline time point; t6, time point after six months of exercise. (a) The mean volume changes per subfield within each exercise group from time point t0 to t6 are shown. The shadowed area represents the 95% confidence interval. (b) The individual volume changes per subfield within each exercise group from time point t0 to t6 are displayed.

Thirdly, the potential effects of aerobic exercise on the HF may not be observable as a whole, but rather via subfields CA1, CA2/3, CA4 and DG, as indicated by our present preliminary study data. Accordingly, previous evidence indicates that different areas of the CA were particularly responsive to aerobic fitness and exercise

(Maurus et al., 2022a; Woodward et al., 2018), whereas the subiculum, for example, was not (Damme et al., 2022). Moreover, there may also exist a hemisphere-specific effect of aerobic exercise on HF volume (Firth et al., 2018; Li et al., 2017). With regard to the underlying mechanisms, beneficial structural adjustments

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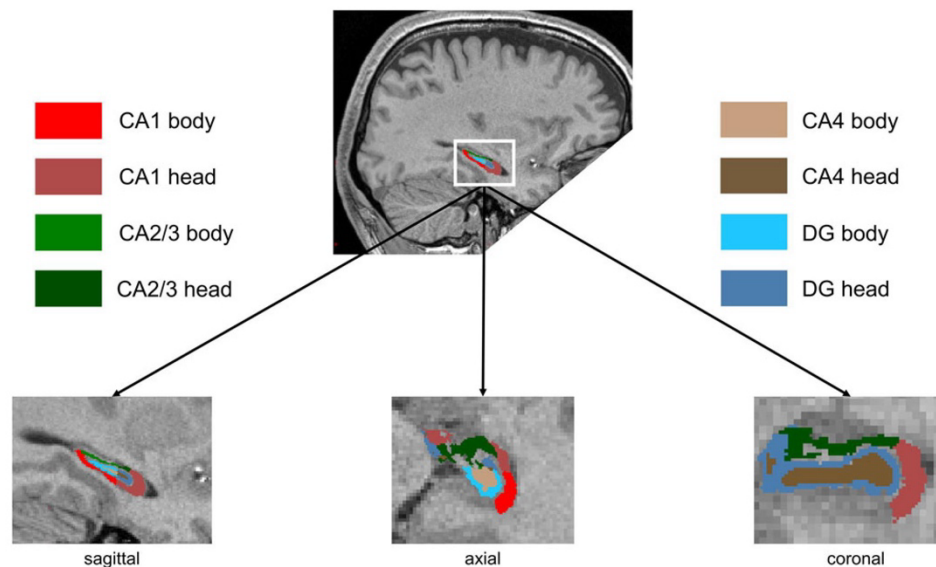


Figure 4. Hippocampal formation subfields. Sagittal (left), axial (middle) and coronal (right) view of the segmentation of CA1–4 and the DG. The subiculum is not displayed because no exercise effects were observed in this case. CA1–4 and DG are separated into head and body in this figure, but volumes from both parts were summed up for the statistical analysis. Images were acquired at a spatial isotropic resolution of 0.8 mm³ at study site Munich and 1 mm³ at study sites Mannheim and Berlin. CA, cornu ammonis; DG, dentate gyrus.

within the HF may result from several exercise-induced neural adaptations such as upregulations of neurotrophic factors, facilitated neuroplastic processes including neurogenesis, angiogenesis and gliogenesis or increases in dendritic density and length (Kandola, Hendrikse, Lucassen, & Yücel, 2016; Liu & Nusslock, 2018; Maurus et al., 2019). Additionally, ameliorations of physical health after aerobic exercise treatment (Vancampfort et al., 2015) may modulate neural plasticity in the HF subfields. Particularly, impaired physical and metabolic health plays a substantial role in schizophrenia (Tian et al., 2023) and thus can lead to widespread neural deteriorations in both brain structure and function (Herrmann, Tesar, Beier, Berg, & Warrings, 2019; Li et al., 2022; Parsons, Steward, Clohesy, Almgren, & Duehlmeier, 2022; Syan et al., 2021). Improving physical and metabolic health through aerobic exercise treatments may thus yield the potential to stimulate regenerative processes in relevant brain regions such as the HF. Considering that CA subfields are especially prone to volume loss in schizophrenia (Ho et al., 2017; Park et al., 2021), it remains particularly important to emphasize that exercise-induced volume increases are assumed to be restorative in their nature, thereby counteracting age- and/or disorder-dependent volume decline (Firth et al., 2018; Li et al., 2017). However, as indicated by our data, the group effect of volume increases in the CA and DG is mainly driven by a few subjects in the aerobic exercise group that show particularly pronounced volume increases (Fig. 3b). This suggests that there is a subgroup of patients with schizophrenia that is specifically responsive to aerobic exercise, potentially modulated by lower general polygenic risk for schizophrenia and a higher genetic burden associated with oligodendrocyte

precursor cells and radial glia (Papiol et al., 2017, 2019). Importantly, more large-scale exercise trials in people with schizophrenia are required to identify stable subgroups of patients that consistently show increased neuroplasticity in the CA and DG after aerobic exercise. To conclude, aerobic exercise potentially mitigates neurodegeneration of one of the most affected HF subfields in people with schizophrenia, at least for a subgroup of patients.

Structural decline of the HF and its subfields is associated with severe cognitive impairments and schizophrenic symptoms (Antoniades et al., 2018; Haukvik et al., 2018; Ho et al., 2017; Khalil et al., 2022; Nakahara et al., 2018, 2020; Pijnenborg et al., 2020). Persistent cognitive deficits prevent long-term improvements in the patients' social and occupational functioning and thus contribute to an unfavorable disease outcome (Green, 2016). In this regard, current large-scale evidence appears promising, demonstrating that exercise treatments improve both cognitive functioning (Dauwan et al., 2016; Fernández-Abascal et al., 2021; Korman et al., 2023) and daily life functioning (Dauwan et al., 2016; Fernández-Abascal et al., 2021; Korman et al., 2023) in schizophrenia. Given the aforementioned link between structural decline within the HF and clinical and cognitive symptoms in schizophrenia, we expected individual-specific HF volume changes post exercise intervention to be linked to changes in clinical outcomes. However, we did not observe said effects, thereby contradicting previous studies suggesting volume increases in the HF to be linked to improvements in short-term memory and global functioning (Falkai et al., 2021; Pajonk et al., 2010). As corresponding evidence in people with

schizophrenia is still limited, we cannot yet derive definite conclusions regarding the clinical relevance of exercise-induced structural adaptations of the HF. Because the stable detection of brain-behavior associations in general requires well-powered large-scale studies, those are needed to clarify the clinical implications of aerobic exercise-induced increases in HF subfield volumes in people with schizophrenia. Thereby, future trials should include comprehensive HF-related cognitive test batteries, covering domains such as episodic or visuospatial memory.

Limitations of this study include that the conclusions regarding the HF subfields are preliminary and require further replication in a larger independent sample. As the MRI assessments were not part of the primary endpoint of the ESPRIT C3 study (for details see Maurus et al. (2020) and Maurus et al. (2023)) and thus were not financially compensated, only a subgroup of patients agreed to participate. Consequently, future studies should ensure adequate financial compensation for patients undergoing MRI assessments since reservations and fears regarding this method are particularly pronounced in schizophrenia. Furthermore, the FreeSurfer segmentation strategy for the HF subfields based on MRI scans at a spatial isotropic resolution of 1 mm³, as applied at study sites Mannheim and Berlin, has been criticized due to issues regarding the detection of the boundaries between subfields (Wisse et al., 2021). However, we still observe distinct patterns of volume increases within the HF when subdividing it only into head, body, and tail, which is less prone to bias. Moreover, the current data basis was not sufficient to identify subgroups of people with schizophrenia who show pronounced volume increases after aerobic exercise. Lastly, methodological differences across the considered exercise studies in schizophrenia complicate a reasonable quantitative approach to summarize findings regarding the clinical relevance of potential HF volume changes in response to aerobic exercise.

In sum, we conclude that aerobic exercise interventions in people with schizophrenia do not lead to significant increases in the total HF volume on the population level. However, our study provides preliminary evidence that aerobic exercise may lead to increases in specific subfields of the HF, namely CA1, CA2/3, CA4, and DG. Large-scale aerobic exercise studies in people with schizophrenia are required to further investigate said effects of aerobic exercise on HF subfield volumes, to identify subgroups of patients that respond particularly well to aerobic exercise, and to elucidate the clinical implications of volume changes within the HF.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0033291724001867>

Data availability statement. The data that support the findings of this study are available on request from the corresponding author, LR. The data are not publicly available because it contains information that could compromise the privacy of research participants. All analysis scripts and documentation sheets will be published on OSF (DOI 10.17605/OSF.IO/TR3NX). A preprint is available under <https://doi.org/10.31219/osf.io/y2phs>.

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Author contributions. AH, BM, AS, AML, PF: funding, conceptualization, and study design; IM, AR, ES, CET, Chu, BV, WT: recruitment of study participants; IM, LR, IP, SM, ES, CET, BV, Chu, AR: data assessment, supervised by HW; BW, KH, DH, ML, KKV, SMO, DG: conduction of exercise trainings, data assessment; IM, LR, TF: interpretation of data. LR and TF: conduction of statistical analyses supervised by TSA. IM, LR and TF: manuscript writing. DK: supervision in neuroimaging data analysis. BP and LR: Conduction of MRI measurements. SS and BEW: Ensuring of optimal imaging conditions at the Department of Radiology of the LMU Hospital. All authors were involved in revising the article and read and approved the final version of the manuscript.

Competing interests. AS was an honorary speaker for TAD Pharma and Roche and a member of Roche advisory boards. AH is an editor of the German (DGPPN) schizophrenia treatment guidelines and first author of the WFSBP schizophrenia treatment guidelines; he has been on the advisory boards of and has received speaker fees from Janssen-Cilag, Lundbeck, Recordati, Rovi, and Otsuka. PF is a co-editor of the German (DGPPN) schizophrenia treatment guidelines and a co-author of the WFSBP schizophrenia treatment guidelines; he is on the advisory boards and receives speaker fees from Janssen, Lundbeck, Otsuka, Servier, and Richter. AML has received consultant fees from Boehringer Ingelheim, Elsevier, Brainsway, Lundbeck Int. Neuroscience Foundation, Lundbeck A/S, Sumitomo Dainippon Pharma Co., Academic Medical Center of the University of Amsterdam, Synapsis Foundation-Alzheimer Research Switzerland, IBS Center for Synaptic Brain Dysfunction, Blueprint Partnership, University of Cambridge, Dt. Zentrum für Neurodegenerative Erkrankungen, Zürich University, Brain Mind Institute, L.E.K. Consulting, ICARE Schizophrenia, Science Advances, Foundation FondaMental, v. Behring Röntgen Stiftung, The Wolfson Foundation, and Sage Therapeutics; in addition, he has received speaker fees from Lundbeck International Foundation, Paul-Martini-Stiftung, Lilly Deutschland, Atheneum, Fama Public Relations, Institut d'investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Janssen-Cilag, Hertie Stiftung, Bodelschwingh-Klinik, Pfizer, Atheneum, University of Freiburg, Schizophrenia Academy, Hong Kong Society of Biological Psychiatry, Fama Public Relations, Spanish Society of Psychiatry, Italian Society of Biological Psychiatry, Reunions I Ciencia S.L., and Brain Center Rudolf Magnus UMC Utrecht and was awarded the Prix Roger de Spoelberch grant and the CINP Lilly Neuroscience Clinical Research Award 2016. BEW is a central radiology reader for Bayer Healthcare and her spouse is an employee of Siemens Healthineers. LR, TF, DK, BP, ML, IP, DG, SM, TSA, ES, CT, BV, SM, CH, AR, KKV, BW, SS, KH, BW, WT, HW, DH and IM report no conflicts of interest.

Clinical trials registration. The underlying study of this manuscript was registered in the International Clinical Trials Database, ClinicalTrials.gov (NCT number: NCT03466112, <https://clinicaltrials.gov/ct2/show/NCT03466112?term=NCT03466112&draw=2&rank=1>) and in the German Clinical Trials Register (DRKS-ID: DRKS00009804).

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5. Paper II



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Reasons to move—a cross-sectional study to identify factors promoting regular exercise

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Regular physical activity can prevent various physical and mental illnesses or improve their prognosis. However, only about half of the German population meets the WHO recommendations for physical activity. The aim of this study was to identify factors that influence engagement in regular exercise and could help increase physical activity levels in the general population. To this end, we conducted a cross-sectional study using questionnaire instruments and self-designed items. The research cohort comprised a sample of online-acquired data from 1,119 mentally healthy individuals. Higher regular exercise was associated with higher both intrinsic and extrinsic motivation, self-efficacy, resilience, internal locus of control, and risk-taking behaviour, as well as higher scores in the personality traits conscientiousness, extraversion, and agreeableness. Higher regular exercise was also linked to lower external locus of control. Whether participants exercised was also related to external circumstances, such as their financial situation, whether family members frequently exercised during childhood or the availability of sports facilities. Furthermore, participants' preferred exercise environment was found to be different from reality. Despite expressing a preference for outdoor and group exercise, most participants reported exercising alone and indoors. People who exercised regularly during childhood stated higher levels of intrinsic as well as extrinsic motivation and resilience. Based on our findings, we suggest that additional low-threshold, low-cost opportunities for physical exercise should be provided in public spaces that lack exercise facilities, as well as in childcare settings with a particular focus on disadvantaged social groups.

KEYWORDS

physical exercise, motivation, personality traits, self-efficacy, cross-sectional study, online survey, general population

1 Introduction

Approximately 10% of all deaths in Europe are due to physical inactivity (1). This makes it one of the top 5 causes of death as it contributes to the development of cardiovascular, metabolic and musculoskeletal diseases (1). Physical inactivity also has a detrimental financial impact on health care systems worldwide, with an estimated cost of \$ 47.6 billion per year between 2020 and 2030 (\$502 billion in total over the decade) (2).

Abbreviations

ASKU, general self-efficacy short scale; BFI-10, big five inventory 10; BMI, body-mass-index; BRS, brief resilience scale; EMI-2, exercise motivation inventory 2; GPAQ, global physical activity questionnaire; IE-4, internal-external control belief scale; SSA, self-efficacy for sporting activity; R1 score, brief scale for risk taking.

Therefore, the World Health Organization (WHO) recommends that adults engage in at least 150 min of moderate physical activity or 75 min of vigorous physical activity per week (3).

Regular physical activity has a wide range of benefits for both physical and mental health: On the one hand, it reduces the risk for myocardial infarction, cardiovascular disease in general, diabetes, and colorectal cancer (4, 5). On the other hand, it can be a preventative measure for common mental health conditions such as depression and anxiety and also has a beneficial effect on these conditions (6). Overall, mortality rates are reduced by up to 30% in people who engage in at least some physical activity compared to people who do not move at all (7, 8). However, according to national surveys, only 45%–51% of the adult population in Germany met these recommendations in 2019/2020 (9) and only 32% of the adult population in the European Union (10). Therefore, it is a desirable objective to increase the level of physical activity in the population, and hence reduce the morbidity and mortality.

Whether people ultimately avoid physical activity, engage in regular exercise, or even achieve peak performance as competitive athletes is largely attributed to the presence or absence of motivation in everyday life (11). Motivation can be described as the drive to achieve a goal that is perceived as valuable (12). Thus, if persons evaluate the target state of exercise positively, for example by recalling feelings of reward and stress relief, they are more likely to exercise to achieve said state. However, if the target state is evaluated negatively (e.g., due to sore muscles after training) the action is more likely to be avoided and, consequently, the individual may cease to exercise (11).

The self-determination theory proposes that an individual's basic needs include competence (self-efficacy), social relatedness, and autonomy (13). It further includes six so-called mini-theories that explain different aspects of motivation or personality functioning. These mini-theories suggest that the fulfilment of these basic needs has a positive influence on motivation, which in turn has a positive effect on physical activity. The mini-theories also differentiate between intrinsic and extrinsic motivation (13). Intrinsic motivation is present when an action is driven by a person's own will. In other words, when the means (action) and the ends (goal of action) are thematically congruent (14). Intrinsic motives may include both the performance of an activity (e.g., kinesthetic experiences) and the achievement of a result dependent on the activity (e.g., a new personal best) (14). In contrast, extrinsic motivation is present when an action is performed due to the anticipation of an aftereffect (e.g., money or recognition) (14). Meaning, the action is the result of an external influence (15, 16). Both intrinsic and extrinsic motives may coexist in any person (14). Previous studies conducted indicate a positive association between levels of intrinsic motivation and high physical activity (17, 18).

However, other factors such as personality traits and self-efficacy also seem to impact physical activity (19, 20). Furthermore, motivation for physical activity has been found to be influenced by various factors, such as a supportive environment or self-efficacy (11, 14). There is also some evidence to suggest that different personality traits may be linked to exercise behaviours (19) and also may impact motivation (21).

Nevertheless, the current knowledge of the factors promoting and/or hindering physical activity is still scarce and incomplete.

There is a paucity of studies that have examined various factors such as motivation, personality traits, and in particular childhood sport history in the same group of subjects in a large-scale study population. Thus the aim of this study is to identify the principal factors that promote regular exercise.

To do this, we investigated the relationship between personality traits and intrinsic as well as extrinsic motives with the type and quantity of physical exercise engaged in. Higher intrinsic and extrinsic motivation was hypothesised to be associated with more frequent exercise. In line with self-determination theory, we also asked about self-efficacy, which corresponds to the basic need for competence; locus of control, which corresponds to the basic need for autonomy; and preference and actual setting for group exercise, which provides at least some insight into the fulfilment of the basic need for social relatedness.

Furthermore, this study explored associations between exercise behaviour during childhood and adolescence and the type as well as the amount of current physical activity. The hypothesis was that regular physical exercise and family support during childhood would be positively associated with regular physical exercise as an adult.

Additionally, this study evaluated facilitators and barriers to regular exercise and examined the impact of the resilience of study participants and their (sport-related) self-efficacy on the presence of physical exercise. It was anticipated that individuals with higher resilience and self-efficacy would be more likely to engage in physical exercise.

These findings can provide insights into how to improve conditions for regularly engaging in physical exercise and how to tailor interventions addressing related and relevant characteristics of respective participants.

2 Methods

2.1 Study design, population, and data extraction

Our study was approved by the local ethics committee of the Faculty of Medicine at the LMU Munich (registration number: 22-0625 KB) and complied with the Declaration of Helsinki.

This cross-sectional study was conducted in Germany using an anonymous questionnaire that could be completed online from any internet-enabled device via the online survey tool "SoSciSurvey" (22).

Inclusion criteria comprised being at least 18 years of age and prior informed consent regarding data collection. People with different levels of physical activity were surveyed, including professional athletes. There was no prior selection. Participants were recruited in a variety of ways, including emails to sports clubs and sport associations, clinics, students, and staff at the LMU Hospital Munich, social media (e.g., facebook groups for leisure swimmers), as well as well visibly placed flyers or posters on campus and in medical facilities. They had the chance to win one of 20 vouchers worth 20€ each. The recruitment period was between August 1st 2022 and December 18th 2022.

Upon completion of the survey, we categorised study participants into two groups according to whether they reported ever having been diagnosed with a mental illness or not. Separately, we identified a group of professional athletes who were members of a cadre with at least four training sessions per week and who participated in competitions such as world championships and Olympic Games. In this analysis, we focus on the sample of individuals who did not report a history of mental illness and were not professional athletes, i.e., the mentally healthy sample as detailed below.

2.2 Questionnaire

The questionnaire included standardised items on socio-demographic history and self-constructed items on physical and mental medical history and on detailed exercise history, both at present and during childhood. Data on body height and body weight were collected in order to calculate the body mass index (BMI). To further assess respondents' current weekly average of engaging in physical activity, the questionnaire also contained the Global Physical Activity Questionnaire (GPAQ) (23). Furthermore, the questionnaire inquired about barriers and facilitators for the implementation of physical exercise.

In addition, the following standardized instruments were implemented: The "Sport- und Bewegungsbezogene Selbstkonkordanz-Skala" (SSK scale) (24) surveyed different motives for exercising and the "SSA scale" (25) measured "self-efficacy for sporting activity". To investigate the different motives of intrinsic and extrinsic motivation as important factors for physical activity according to the self-determination theory (13), we applied the "Exercise Motivations Inventory" (EMI-2; used in an abbreviated form) (26).

The Big Five Inventory 10 (BFI-10) (27) was used to survey the five dimensions of personality traits (extraversion, conscientiousness, agreeableness, neuroticism and openness). The Internal-External Control Belief Scale (IE-4) (28) was used to assess internal and external loci of control (the extent to which someone believes that the occurrence of an event is dependent on or independent of their own behaviour), and the General Self-Efficacy Short Scale (ASKU) (29) was used to assess general self-efficacy. Furthermore, the Brief Resilience Scale (BRS) (30) and the Brief Scale for Risk Taking (R1) (31) assessed resilience and risk affinity, while the Sport-Related Support Scale (32) evaluated support from friends and family. Reliability and validity information for the psychometric instruments used can be found in [Supplementary S1](#).

The questionnaire contained up to 190 questions and took about 20 min to complete. Depending on the information provided by the study participants, certain questions were automatically hidden or shown, providing further information on previous items (the full translated questionnaire can be found in [Supplementary Table S2](#)).

2.3 Statistical analyses

The descriptive preliminary analysis was carried out using Microsoft Excel version 16.73 (33). At first, we categorized the

mentally healthy sample into an exercising and a non-exercising group. Said classification was based on the notion of whether respondents currently exercised regularly (at least once each week). This classification did not consider occupational activities or distances travelled by foot or by bicycle that were not undertaken for the purpose of physical exercise. Similarly, we classified participants depending on whether they engaged in regular exercise during childhood or not, irrespective of physical education classes in school.

IBM SPSS version 29.0.0.0 (34) was used for further analysis and to characterise our sample by frequencies, means, medians and standard deviations. It was also used to calculate the participants' body-mass-index (BMI) as ratio of body weight in kilograms to height squared in meters.

To compare two different groups - for example, those who exercise and those who do not - we used independent *t*-tests for metric data, Cohen's *d* to measure the effect size of significant results and the Welch method to correct for unequal variances. Mann-Whitney *U*-tests and Chi-Square-tests were used for non-metric data. We also used binary logistic regression to examine the influence of a personality trait on the likelihood of regular exercise or to examine the influence of social support on the likelihood of regular exercise. Pearson correlations were performed for metric data and Spearman correlations for non-metric data. A distinct quantity of responses (*n*) was available for each question, which can be identified by the degrees of freedom (df).

3 Results

3.1 Demographic characteristics

1,746 people gave their informed consent and started to participate in the survey, of whom 1,577 responded to at least the sociodemographic and somatic history questions and were therefore included in our analysis. 1,376 participants completed the entire questionnaire. This publication focuses on the 1,119 individuals without a known history of mental illness, here referred to as the mentally healthy sample. The remaining 458 participants were either professional athletes or reported having been diagnosed with a mental illness.

The mean age in our mentally healthy sample was 38.3 ± 15.5 years, 66.5% (*n* = 744) were female and 33.5% (*n* = 375) male. Most respondents had the highest German school degree: 68.0% (*n* = 761). Financial worries were reported by 7.1% (*n* = 80) of the mentally healthy sample. A detailed characterisation of participants can be found in [Supplementary Table S3](#).

3.2 Determining factors of exercise behaviour

Overall, 73.1% (*n* = 754) of the mentally healthy sample reported to engage in regular exercise at the time of the study, 70.2% of the female participants and 78.6% of the male

participants. Most exercised one to three times a week (58.3%), 29.3% exercised 4–5 times and 12.4% exercised six times or more. For details on the participants' levels of physical activity as assessed with the GPAQ (23) see Table 1. In our exercising group, 92.7% met the WHO recommendations of taking part in at least 150 min of physical activity each week, 89.9% through leisure activities alone. In comparison, in our non-exercising group, only 51.8% met the WHO recommendations. Overall, the WHO recommendations were met by 81.8% of our mentally healthy sample. See Table 1 for more information about the participants' daily physical activity levels. Those who exercised regularly reported a slightly lower Body-Mass-Index (BMI) than our non-exercising group (23.31 vs. 24.55 kg/m²; $p < 0.001$, $t(393) = 3.94$, MD = 1.24, Cohen's $d = 3.92$, 95% CI [0.18, 0.46]).

The mean age in the exercising group was 39.01 years (SD = 15.99) and 37.34 years (SD = 14.33) in the non-exercising group. There was no significant correlation between age and exercise behaviour nor did exercise behaviour differ based on

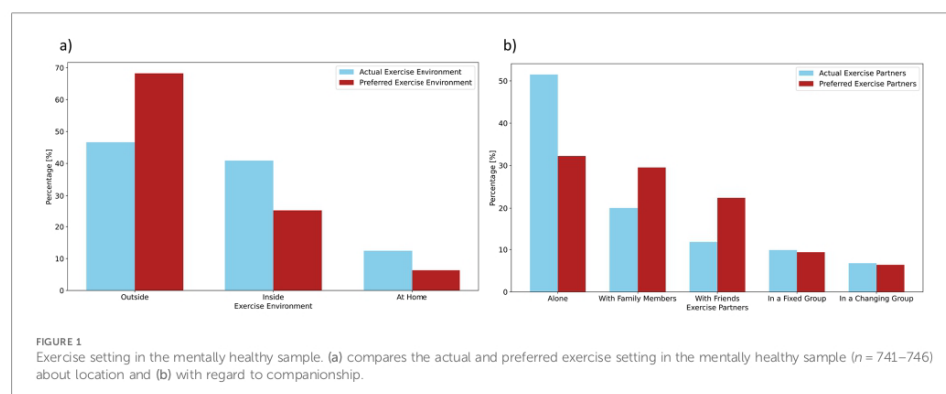
participants' income. However, we found a significant difference between the two groups regarding the subjectively reported variable "health status" ($U = 84,260.5$, $Z = -4.79$, $p < 0.001$) as well as for the variable "highest educational attainment" ($U = 97,292.5$, $Z = -2.00$, $p = 0.045$). Both variables showed higher values in the exercising group.

As illustrated in Figure 1, most of the mentally healthy sample (68.3%) reported a preference for exercising outdoors, whereas only 46.6% actually do so. Similarly, indoor, and at-home sports are practised much more frequently than theoretically preferred. There are also clear differences between preferred and actual levels of companionship. Although more than half of the mentally healthy sample (51.5%, $n = 383$) reported mostly exercising alone, the majority actually expressed a preference to exercise with friends [32.2% ($n = 239$)] or in a group [28.8% ($n = 214$)], whereas only 29.6% ($n = 220$) favoured exercising alone. Overall and noteworthy, discrepancies between preferred and actual settings were significant.

TABLE 1 Daily physical activity levels as assessed by the GPAQ.

	Descriptive statistics - mean (SD)			t-test: comparison between exercising sample and non-exercising sample					
	Total mentally healthy sample ($n = 1,119$)	Exercising sample ($n = 754$)	Non-exercising sample ($n = 278$)	p	df	T	MD	Cohen's d	95% CI
Daily moderate leisure activity in minutes	19.1 (25.8)	23.7 (27.5)	12.1 (20.4)	<0.001	665	-7.33	-11.58	25.81	[-0.59, -0.31]
Daily intensive leisure activity in minutes	22.1 (34.0)	30.7 (37.6)	4.8 (12.4)	<0.001	1,021	-16.61	-25.90	32.80	[-0.93, -0.65]
Daily moderate work activity in minutes	19.2 (51.9)	19.6 (51.7)	22.5 (57.0)	0.224					
Daily intensive work activity in minutes	7.8 (43.1)	5.8 (27.8)	8.1 (43.8)	0.207					
Daily total activity in minutes	68.2 (97.3)	79.9 (92.8)	47.5 (99.0)	<0.001	1,030	-4.88	-32.35	94.53	[-0.48, -0.20]
Daily transport activities in minutes	23.9 (29.6)	25.8 (29.1)	25.2 (32.6)	0.415					
Daily sitting in minutes	457.3 (649.6)	492.1 (724.7)	510.9 (454.6)	0.344					

Table 1 presents descriptive statistics for the GPAQ for the total mentally healthy sample, the exercising sample and the non-exercising sample and a comparison of means using an independent t -test between the exercising and non-exercising group. GPAQ, Global physical activity questionnaire (23), SD, standard deviation.



3.2.1 Personality traits in the mentally healthy sample

We further investigated whether the personality traits extraversion, conscientiousness, agreeableness, neuroticism, and openness as evaluated with the BFI-10 (27) were associated with the participants' exercise behaviour as well as preferred setting and kind of exercise.

Independent *t*-tests and binary logistic regressions showed that the personality trait conscientiousness ($p < 0.001$, $t(998) = -7.55$, MD = -0.42, Cohen's $d = 0.78$, 95% CI [-0.68, -0.40]) (OR = 0.95), as well as the traits extraversion ($p = 0.022$, $t(998) = -2.29$, MD = 0.17, Cohen's $d = 1.01$, 95% CI [-0.30, -0.02]) (OR = 0.17), and agreeableness ($p = 0.022$, $t(997) = -2.30$, MD = -0.131, Cohen's $d = 0.802$, 95% CI [-0.30, -0.02]) (OR = 0.22) were significantly related to whether or not a participant engaged in regular exercise (see Figure 2 for violin plots). Namely, participants who exhibited a stronger expression of these traits were more likely to engage in regular exercise. However, there was no significant association between the personality traits neuroticism or openness and exercise behaviour. Within the group of regular exercisers, higher levels of conscientiousness correlated positively with exercise frequency ($r = 0.16$, $p < 0.001$, $n = 729$) (see Figure 3 for violin plots).

In terms of exercise setting, people who exercised with others rather than alone had higher levels of agreeableness ($p = 0.046$, $t(723) = -2.00$, MD = -0.12, Cohen's $d = 0.78$, 95% CI [-0.29, -0.002]). No notable distinctions in other personality traits were observed between those groups.

We also found no discernible correlations between personality traits and the preferred kind of sports.

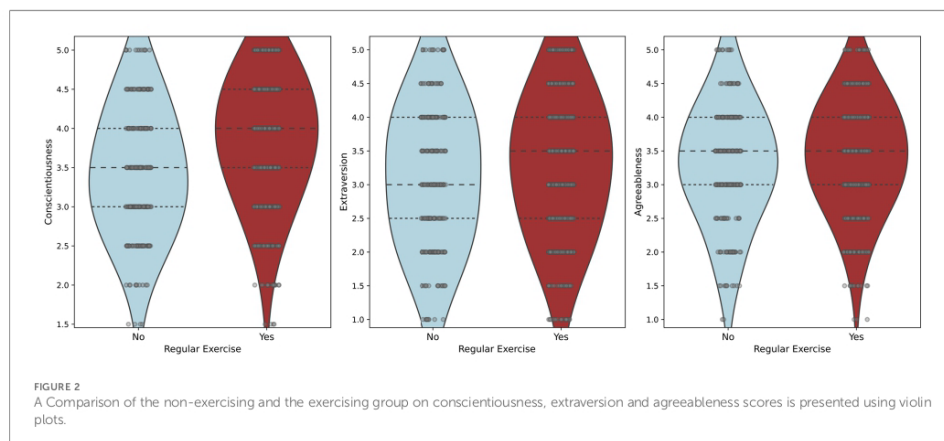
In conclusion, we observed that regular exercise was most closely linked to the personality traits extraversion, conscientiousness, and agreeableness. Conscientiousness was also significantly related to the frequency of exercise and agreeableness to the setting of exercise.

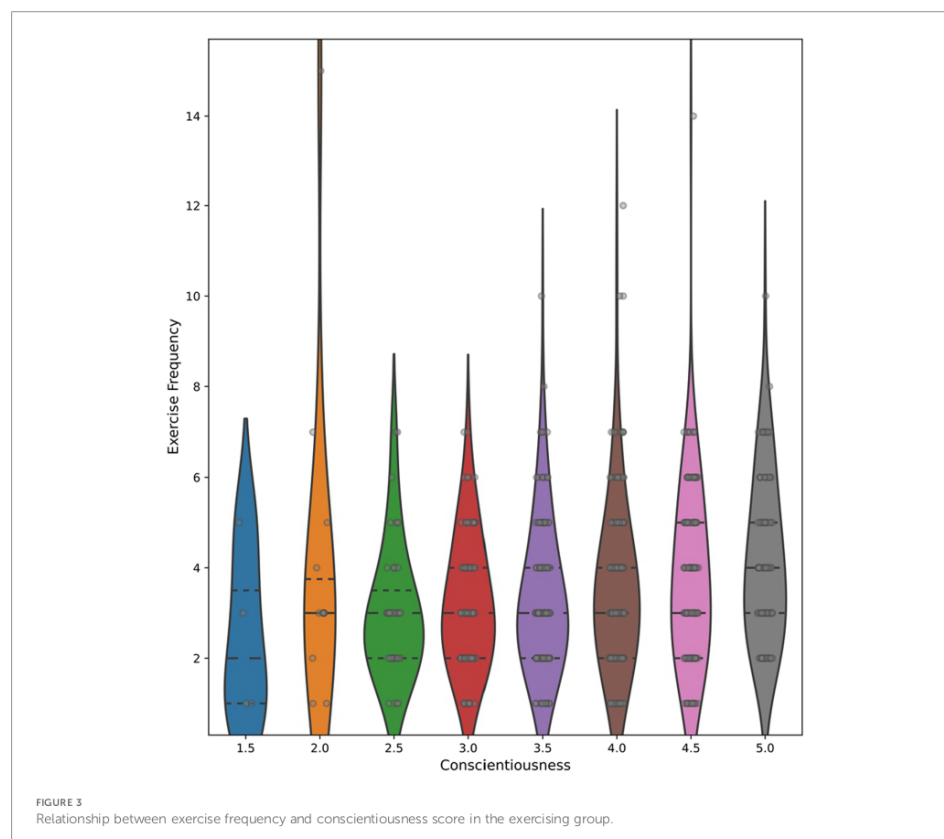
3.2.2 Self-efficacy, locus of control, resilience and risk taking

We also evaluated if engaging in regular exercise was associated with increased levels of self-efficacy, an internal locus of control, and resilience scores. Our results showed that the exercise group had significantly higher ratings in both general self-efficacy (ASKU score) ($p = 0.002$, $t(995) = -3.09$, MD = -0.13, Cohen's $d = 0.59$, 95% CI [-0.36, -0.08]) and sport-related self-efficacy (SSA score) ($p < 0.001$, $t(402) = -15.37$, MD = -1.41, Cohen's $d = 1.17$, 95% CI [-1.35, -1.05]), a rather internal locus of control (IE-4 score) ($p < 0.001$, $t(996) = -4.24$, MD = -0.193, Cohen's $d = 0.64$, 95% CI [-0.44, -0.16]) as well as higher scores in resilience ratings (BRS score) ($p < 0.001$, $t(993) = -4.54$, MD = -0.223, Cohen's $d = 0.69$, 95% CI [-0.46, -0.18]) when compared to the non-exercising group. In addition, the exercise group reported higher scores for risk taking (R1 score) ($p < 0.001$, $t(428) = -3.64$, MD = -0.25, Cohen's $d = 0.91$, 95% CI [-0.42, -0.14]). By contrast, an external locus of control was more pronounced in the non-exercising group (IE-4 score) ($p < 0.001$, $t(447) = 3.70$, MD = 0.21, Cohen's $d = 0.76$, 95% CI [0.13, 0.41]). The corresponding violin plots are shown in Figure 4.

3.2.3 Intrinsic and extrinsic motivation

As hypothesised, we found an association between intrinsic and extrinsic motivation as assessed by the EMI-2 (26) and exercise behaviour in the mentally healthy sample. Both intrinsic and extrinsic motivation were significantly related ($p < 0.001$) to whether a person engages in physical exercise or not (intrinsic: $t(351) = -13.93$, MD = -1.10, Cohen's $d = 0.93$, 95% CI [-1.34, -1.04]; extrinsic: $t(410) = -7.20$, MD = -0.46, Cohen's $d = 0.82$, 95% CI [-0.70, -0.42]). On average, motives related to intrinsic motivation were upwards of 20% more pronounced in the exercising than in the non-exercising group (on a scale of 0–5) (*t*-tests with $p < 0.001$): enjoyment ($t(391) = -16.61$, MD = -1.73, Cohen's $d = 1.30$, 95% CI [-1.48, -1.18]), challenge ($t(998) =$





–12.72, MD = –1.34, Cohen's $d = 1.48$, 95% CI [–1.05, –0.76]), revitalisation ($t(359) = -12.54$, MD = –1.21, Cohen's $d = 1.13$, 95% CI [–1.22, –0.92]), stress management ($t(381) = -11.18$, MD = 1.20, Cohen's $d = 1.31$, 95% CI [–1.06, –0.77]). Moreover, the extrinsic motive affiliation was also higher in the exercising group ($t(525) = -8.67$, MD = –1.05, Cohen's $d = 1.77$, 95% CI [–0.73, –0.45]). The remaining internal (competition, nimbleness, positive health, strength and endurance) and external motives (appearance, ill health avoidance, positive health, social recognition) were between 10% and 20% higher for those who exercised. We found no statistically significant differences for the extrinsic motives of social pressure and weight management.

In conclusion, the most important motives in our study appear to be enjoyment, challenge, revitalisation, stress management and affiliation. Intrinsic motivation seems to be more important than extrinsic motivation when it comes to regular physical exercise.

A detailed summary of the EMI-2 results can be found in [Supplementary Table S4](#), corresponding violin plots in [Figure 5](#).

3.2.4 Social support

Contrary to our assumption, in our mentally healthy sample we found no significant relationship between experiencing exercise-related family support during childhood and the likelihood of engaging in regular exercise in the present. Among those in the mentally healthy sample who exercised in childhood, 70.1% had at least one other exercising family member. In comparison, only 27.1% of the inactive childhood group had an exercising family member.

Thus, it appears that family support itself during childhood does not directly influence an individual's likelihood of exercising regularly, whereas the presence of other exercising family members does.

3.2.5 Facilitators and barriers to regular exercise

Examining the participants' reported barriers and facilitators to regular exercise (or even more exercise in the case of the exercising sample), the main barriers for the physically inactive group were

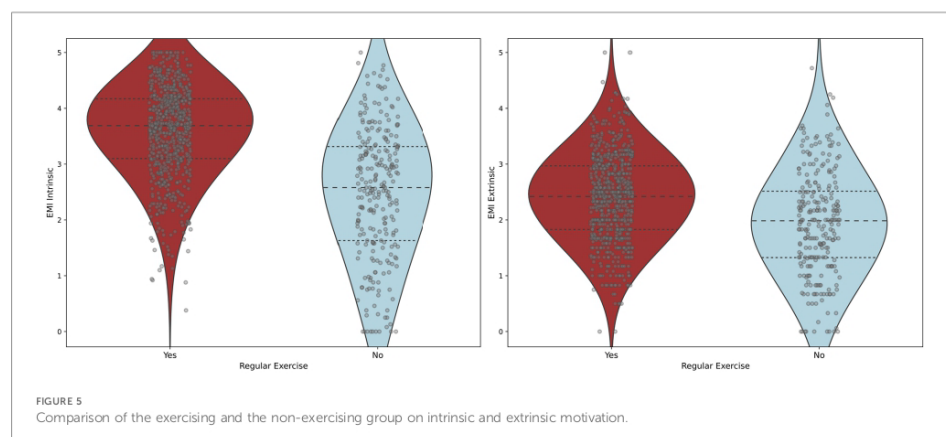
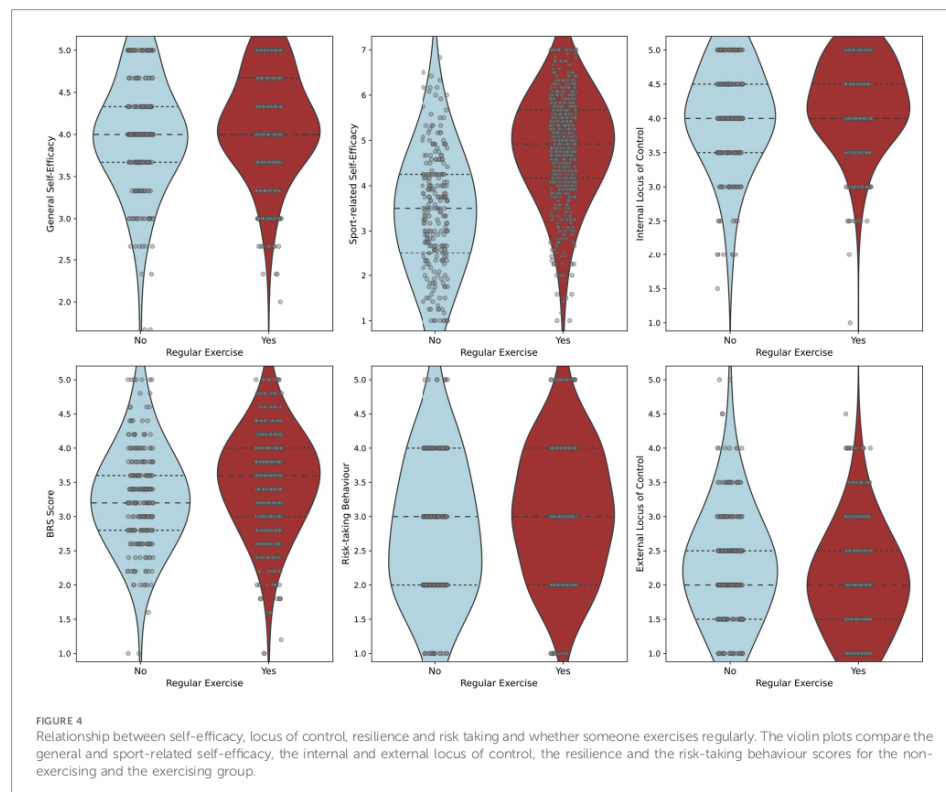


TABLE 2 Barriers to regular exercise.

	Non-exercising sample (<i>n</i> = 252–267)		Exercising sample (<i>n</i> = 693–718)		Mann-Whitney- <i>U</i> -test			
	M	SD	M	SD	<i>p</i>	U	Z	<i>r</i>
Financial barriers	1.89	1.13	1.70	1.00	0.02	86,446.00	–2.32	–0.07
Lack of knowledge	2.46	1.26	1.59	0.87	<0.001	56,961.00	–10.60	–0.34
Missing offer	2.00	1.14	1.61	1.00	<0.001	74,921.50	–5.65	–0.18
Unaware	1.77	1.08	1.28	0.68	<0.001	71,152.00	–7.97	–0.26
No time due to family	2.29	1.36	1.82	1.07	<0.001	77,861.50	–4.80	–0.15
No time due to work	3.14	1.44	2.53	1.32	<0.001	71,394.50	–6.07	–0.19
No time due to other matters	2.50	1.22	1.83	1.01	<0.001	59,878.50	–7.86	–0.26
Too unathletic	2.35	1.28	1.48	0.81	<0.001	56,405.00	–10.93	–0.35
Shame	2.04	1.27	1.44	0.82	<0.001	70,964.00	–7.42	–0.24
Fear of embarrassment	2.09	1.28	1.52	0.88	<0.001	71,851.00	–6.86	–0.22
Concern for injury	1.75	0.98	1.65	0.92	0.125			
Lack of drive and energy	3.38	1.24	2.03	1.04	<0.001	40,640.00	–14.24	–0.45
Pain or discomfort during exercise	1.94	1.19	1.52	0.81	<0.001	78,191.50	–4.95	–0.16
Disappointed by previous experiences	1.95	1.16	1.50	0.83	<0.001	74,177.50	–6.06	–0.19
Bigger worries in life at the moment	2.59	1.38	1.74	0.99	<0.001	61,141.50	–9.11	–0.29

Table 2 shows the barriers to regular (or even more) physical exercise in both the exercising sample (*n* = 693–718) and the non-exercising sample (*n* = 252–267). Participants were requested to assess, on a scale of 1 (does not apply at all) to 5 (fully applies), the degree to which each item listed impeded their exercise behaviour. M, mean; SD, standard deviation.

TABLE 3 Facilitators to regular exercise.

	Non-exercising sample (<i>n</i> = 256–263)		Exercising sample (<i>n</i> = 697–717)		Mann-Whitney- <i>U</i> -test			
	M	SD	M	SD	<i>p</i>	U	Z	<i>r</i>
Further education	2.06	1.12	1.85	1.09	0.002	80,645.00	–3.06	–0.08
Fixed appointments	3.44	1.31	3.42	1.38	0.92			
Flexible training in terms of time and place	3.10	1.27	3.06	1.37	0.71			
Reminder by phone or email	1.94	1.13	1.64	0.99	<0.001	75,475.50	–4.29	–0.13
Short distance to the training location	3.73	1.25	3.83	1.29	0.12			
Trainings free of charge	3.38	1.41	3.26	1.47	0.35			
Group with equally fit people	3.24	1.38	3.13	1.39	0.25			
Coaches with knowledge of physical conditions	2.53	1.43	2.40	1.43	0.19			

Table 3 shows the facilitators to regular (or even more) physical exercise in both the exercising sample (*n* = 697–717) and the non-exercising sample (*n* = 256–263). Participants were asked to assess, on a scale of 1 (does not apply at all) to 5 (fully applies), the extent to which each of the items listed would be helpful in order to increase their amount of physical exercise. M, mean; SD, standard deviation.

lack of time due to work and a lack of drive and energy (see Table 2). Both groups reported that a short distance to the training venue and fixed appointments were reported to be the most helpful (see Table 3).

Of note, study participants with lower scores on the personality trait of conscientiousness gave higher scores for the facilitator “reminders by phone or email” ($r = -0.18$, $p < 0.001$, $n = 957$).

3.2.6 Physical exercise during childhood

To evaluate the impact of exercise during childhood on present outcomes, we additionally gathered data on exercise-related characteristics in childhood. 78% of the mentally healthy sample reported having exercised regularly during childhood (76.9% in women and 80.1% in men). Approximately 80% of

individuals who participated in regular exercise during their respective childhoods were affiliated with sports clubs, with a 78.2% membership percentage below the age of 12 and 81.3% above the age of 12. Interestingly, individuals who exercised regularly in childhood were more likely to maintain their respective exercise habits in adulthood. 76.8% of those who exercised regularly during childhood still exercise regularly today, in contrast to only 60.1% in the comparison group [$\chi^2(1) = 24.39$, $p < 0.001$].

In our study, people who regularly exercised during childhood reported higher levels of education ($U = 90,449.0$, $Z = -3.52$, $p < 0.001$) and income ($U = 90,882.5$, $Z = -2.93$, $p < 0.001$) compared to those who did not. However, we found no difference in subjectively reported current health status or BMI.

3.2.6.1 Relationship between exercise behaviour during childhood and personality characteristics

Individuals who reported regularly engaging in exercise as children scored higher on extraversion ($p < 0.001$, $t(998) = -3.54$, $MD = -0.27$, Cohen's $d = 1.01$, 95% CI $[-0.42, -0.12]$) and lower on neuroticism ($p < 0.001$, $t(998) = 3.94$, $MD = 0.28$, Cohen's $d = 0.94$, 95% CI $[0.15, 0.45]$) than individuals who did not exercise regularly in childhood. Moreover, they showed significantly higher levels of both intrinsic and extrinsic motivation towards exercise ($p < 0.001$, $t(305) = -7.65$ and $t(987) = -4.40$, $MD = -0.28$ and -0.67 ; Cohen's $d = 1.01$ and 0.84 , 95% CI $[-0.81, -0.51]$ and $[-0.49, -0.19]$). In a further comparison of the two groups, we also found significantly higher values of internal locus of control, resilience, self-efficacy and risk-taking for those who engaged in regular exercise during childhood. However, the personality traits agreeableness, conscientiousness, and openness, as well as external locus of control showed no significant difference.

3.2.6.2 Discontinuation of sport in childhood

More than two-thirds (69.0%) of participants from the mentally healthy sample reported cessation of participation in a sport during childhood/adolescence. The most common reason given by 42.0% (multiple choice) was "other hobbies were more important". The second most common reason was "no fun", given by 36.0%. The reasons "didn't get on with coach", "too much pressure to succeed" and "financial reasons" were selected by 8.6%, 6.2%, and 5.3% of participants, respectively.

Over 43.4% of study participants expressed a desire to engage in a certain sport during childhood but the inability to do so. The most common reason for this was "no facilities nearby" with 42.3%, followed by "no family support" with 33.1%, and "financial reasons" with 26.9%.

4 Discussion

This study aimed to identify determinants of exercise behaviour to contribute to a better understanding of how to promote optimal conditions for regular physical activity in the general population. The majority of participants in our study exercised regularly and met the WHO criteria of at least 150 min of moderate physical activity or 75 min of vigorous physical activity per week. While most of the participants reported a preference to exercise outdoors with friends or in groups, the number of individuals actually doing so was significantly lower. While there was no significant correlation between age and exercising behaviour, the presence of different motives and individual personality traits were linked to engaging in regular exercise. Specifically, we observed significant positive associations between exercise behaviour and the personality traits conscientiousness, extraversion, and agreeableness and between exercise behaviour and both intrinsic and extrinsic levels of motivation, with intrinsic motives appearing to play a more important role. In addition, levels of self-efficacy, resilience, internal locus of control and risk taking showed positive

associations with exercise behaviour. However, a significant negative association was found for an external locus of control.

Moreover, people who exercised regularly during childhood had a notably higher proportion of active family members compared to those who didn't exercise as children. Lastly, people who exercised regularly as children were more likely to exercise regularly as adults.

According to previous studies, only about half of the adult population met the WHO recommendations (1, 9), whereas in our sample about 4 out of 5 people did. This might be due to our recruitment being biased towards individuals with a sports-related background or because the topic might have appealed more to sports enthusiasts, resulting in a higher proportion of physically active participants in our study.

Our findings on the relationship between personality characteristics and exercise behaviour are in line with previous literature and said to be independent of factors such as gender, age or culture/country (35, 36). Individuals with high levels of conscientiousness are regarded as disciplined, self-regulated, dutiful, and deliberate (37), which favours the initiation and maintenance of physical exercise. Similarly, people with higher levels of extraversion are more prone to seek out social contact and sensory stimulation (37), which can be a part of engaging in exercise. Those with a higher level of agreeableness are considered to be compassionate, humble, trusting, cooperative, and altruistic (37) which can also be beneficial for maintaining physical exercise. Whereas the positive correlations between physical exercise and the personality traits extraversion, conscientiousness and agreeableness are in line with a recent cross-sectional study conducted in 4,244 German students and with previous meta-analyses (19, 35, 36), our study could not confirm a positive association between physical exercise and the personality trait openness as well as a negative association with neuroticism that has been previously suggested (19, 36). This discrepancy may be attributed to the exclusion of individuals diagnosed with a mental illness, a group known to exhibit elevated neuroticism scores (38). Said results underscore the necessity to tailor exercise regimens to individual needs and personality traits, such as, for example, cues and/or reminders via telephone for people low in conscientiousness. For individuals with low levels of extraversion and/or agreeableness, participation in open settings, such as open days or direct contact in public spaces may be beneficial.

Our finding of a positive association between intrinsic and extrinsic motivation and regular exercise behaviour is consistent with previous research (39). The motives rated as most significant in our exercising sample – enjoyment, stress management, challenge, revitalisation and affiliation – are also among the most commonly reported motives in other studies (40, 41). If prevention is to be further strengthened in the German health care system, it would be important to start with these motives. The keywords enjoyment, stress management, challenge, revitalisation and affiliation can be used to draw attention to exercise programs, promote workplace exercise and target health insurance members. Exercise regimens could be planned in cooperation with those concerned, thereby increasing intention to

exercise. Previous studies have shown that motivation can be influenced by using behaviour change techniques. These behaviour change techniques may include, for example, behavioural goal setting, action planning, behavioural feedback, behavioural instruction, or behavioural demonstration (42).

Other studies also found a positive relationship between self-efficacy and exercise behaviour (43). Intervention studies have used a variety of methods to increase self-efficacy levels, such as face-to-face and telephone counselling, email feedback, discussion groups or behaviour change classes. They have shown small but significant effects on self-efficacy and subsequently on physical activity levels, focusing mainly on lifestyle physical activity such as walking and gardening (43). Future research should build on this to identify further effective interventions to increase self-efficacy and, therefore, exercise and physical activity in the general population.

In our study, people who exercise regularly show increased self-efficacy, a stronger internal locus of control and higher overall and intrinsic motivation compared to non-exercisers. In addition, the majority of our study population prefer to exercise with others rather than alone. This is consistent with the self-determination theory (13).

Regarding additional barriers and facilitators of regular exercise, many participants indicated that proximity as well as flexible training times and locations would be helpful. Correspondingly, the most common reason given for not exercising regularly during childhood was a lack of sports facilities in the area. To address this, more low-threshold public exercise opportunities should be provided in public areas and where few sports facilities exist. This could be achieved by the establishment of weekly exercise groups at different levels that can be joined without prior registration and free of charge. The construction and maintenance of public fitness facilities like outdoor gyms, safe and accessible cycle paths and public parks could also animate people and encourage them to spend more time outdoors exercising. Accordingly, a study conducted in Chile found that the presence of more outdoor gyms increases the physical activity in the population and increases the likelihood of meeting the WHO recommendations for physical activity (44).

Low-threshold and low-cost or no-cost opportunities in childcare facilities should also be created and promoted, especially for those from socially disadvantaged backgrounds, as these children generally have less opportunity to engage in physical activity (45). Our data supports this notion as many individuals reported not engaging in or quitting their preferred sport due to a lack of financial resources. A Brazilian study found that the majority of outdoor gym users were people with low income, so the installation of outdoor gyms could reduce social inequalities in physical exercise (46).

Another approach would be to introduce and promote more free, well-developed fitness apps, supported, for example, by health insurance bonus programs. This would have the advantage of being flexible in terms of place and time, but the disadvantage of losing the social aspect of exercise, which also seems to play an important role, as most of our study

participants stated that they prefer to exercise with others rather than alone.

Our data also shows a significant association between the exercise behaviour of family members and respondents during their respective childhoods. Moreover, engaging in regular exercise during childhood seems to make regular exercise more likely in the present. Thus, the exercise behaviour of family members appears to have a significant and lasting influence on exercise levels of people in child- and adulthood. In conclusion, exercise interventions, particularly those targeting family members could be beneficial to increasing physical activity levels in the population. Establishing programs parents and children attend together could be a possible solution to said problem.

When interpreting our findings, several limitations have to be considered. Although the online format of our survey allowed us to reach a large number of participants from different backgrounds, there are constraints within this format. As our survey was predominantly advertised in sporting environments and at universities, our results are not representative of the wider population. It is possible that a sampling bias occurred whereby individuals who are less educated and do not exercise regularly are under-represented. This is also supported by the fact that 68% of participants have the highest German school-leaving qualification. Additionally, self-selection bias towards physically active people as a result of the survey's subject matter may have occurred. Due to the relatively time-consuming design of the questionnaire, 12.7% did not complete the survey, possibly introducing further bias. Additionally, the implementation of self-report instruments in our study poses potential for social desirability and recall biases. The use of self-report alone to classify participants into the mentally healthy group may have introduced diagnostic uncertainty. Expert interviews may be a future way to address this issue in smaller follow-up studies. Finally, the cross-sectional design of our study does not allow us to draw conclusions about the causality of observed relationships.

5 Conclusion

Based on our findings, we recommend that more low-threshold public exercise opportunities (e.g., public fitness facilities) should be provided in public areas with few sports facilities and in childcare facilities. Low-cost exercise opportunities should also be created and promoted, especially for socially disadvantaged groups.

We further observed that the motives enjoyment, stress management, challenge, revitalisation, and affiliation play a crucial role for engaging in regular exercise. Therefore, it is essential to target and strengthen said motives in the general population.

Moreover, interventions to increase (exercise-related) self-efficacy could also be helpful in promoting regular exercise. Future studies should explore the direction of the relationship between personality traits and exercise, and how to best tailor exercise opportunities to the individual needs of exercise participants. We believe that addressing these suggestions in the future can make a significant contribution to promoting exercise,

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which in turn can significantly contribute to improving both physical and mental health in the population.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The project was approved by the local Ethics Committee of the Faculty of Medicine at the LMU Munich (registration number: 22-0625KB).

Author contributions

AW: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Software, Writing – original draft, Writing – review & editing. KK: Conceptualization, Data curation, Investigation, Methodology, Project administration, Writing – review & editing. LR: Formal Analysis, Validation, Writing – review & editing. TF: Writing – review & editing. RS: Visualization, Writing – review & editing. AH: Supervision, Writing – review & editing. AS: Supervision, Writing – review & editing. PF: Resources, Supervision, Writing – review & editing. IM: Conceptualization, Project administration, Resources, Supervision, Validation, Writing – review & editing.

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Conflict of interest

AH was member of advisory boards of Boehringer-Ingelheim, Lundbeck, Janssen, Otsuka, Rovi and Recordati and received paid speakership by these companies as well as by AbbVie and Advanz. He is editor of the German schizophrenia guideline. PF is a co-editor of the German (DGPPN) schizophrenia treatment guidelines and a co-author of the WFSBP schizophrenia treatment guidelines; he is on the advisory boards and receives speaker fees from Janssen, Lundbeck, Otsuka, Servier and Richter.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fspor.2024.1515687/full#supplementary-material>

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